

REMARKS/ARGUMENTS

In the specification, paragraph [0045] has been amended to correct a typographical error and remove reference to hyperlinks and incorporate the indicated publicly available databases by reference in accordance with 37 CFR § 1.57(d).

The Examiner has objected to the presentation of Claim 23 in Applicant's response filed September 5, 2003, because it was not in compliance with 37 CFR § 1.121(c). Since Examiner did not enter an amendment to Claim 23, and, as the insertion of the word "between" in the listing of claims filed with response of September 5, 2003, was an obvious typographical error, Applicants have retained the wording of Claim 23 as presented with Applicants' Amendment filed September 10, 2002.

Claims 15, 22, 28, and 29 have been amended to make explicit that which is clear in the specification, namely the conditions under which the mutated bacteria may be cultured. This amendment is fully supported in the specification, for example at paragraphs [0041] and [0044]. New claim 54 has been added to specifically claim use of quinolone as an antimicrobial. Support can be found in the specification, for example at paragraph [0041]. It is believed that none of these amendments constitute new matter and their entry is requested.

Rejection of Claims Under 35 U.S.C. §112

The Office Action rejects claims 15-41 as indefinite. Specifically, the Office Action states that the basis for the differentiation of "growing" or "non-growing" cultures of bacteria is unclear. In support of this rejection, the Examiner asserts that the description of the invention on page 11 of the specification is inconsistent with Example 4, and that Example 4 is the only example put forth. Applicants respectfully disagree.

Example 4 is not offered as an example of differentiation of growing and non-growing bacteria. Rather, Example 4 provides one exemplary approach that may be used to identify appropriate conditions for culturing the mutated bacteria, such as a concentration of antimicrobial agent, which conditions may then be applied in the practice of the invention. More specifically, the salt solution used in Example 4 (MSS) was utilized to produce stasis conditions ([0074]), and thereby simulate non-growing bacteria. Example 4 provides a comparison of the effect of an antimicrobial agent on a culture of mutated bacteria under growing conditions, with the antimicrobial agent's effect on a culture of the mutated bacteria under non-growing conditions. Thus, Example 4 provides one approach to identify a concentration of antimicrobial which could be expected to kill growing but not non-growing bacteria.

Applicants further note that Example 5 reports culturing bovine macrophages infected with the mutated bacteria of Example 4, in tissue culture medium containing Bay y 3118 at 5X MIC, and the subsequent recovery of surviving bacteria. (Note that Example 4 indicates that Bay y 3118, at 5X MIC, did not kill non-growing bacteria, but had a bactericidal action on growing bacteria (see also Figs. 3A & B)). As such, Example 5 provides an exemplary method for differentiating growing from non-growing bacteria. The recovered surviving bacteria may be tested and non-virulent bacteria selected. Example 7 is illustrative of testing and selection of the non-virulent mutant bacteria.

As further basis for rejection of the claims under 35 U.S.C. § 112, the Office Action states that it is unclear what amount of antimicrobial agent is claimed. It is believed that the amendment of claims herein obviates this rejection. Withdrawal of this rejection is therefore requested. The claims have been rewritten solely for the purpose addressing this rejection under 35 U.S.C. § 112.

The specification provides a detailed teaching which, together with knowledge generally available in the art, describes exemplary methods which may be employed to determine the amount of antimicrobial agent to be used as well as other culture conditions. For example, the specification states at paragraph [0041], "...selection [of the antimicrobial] is based on the ability of an antimicrobial to kill growing mycobacteria while having a reduced or no [a]ffect on non-growing bacteria" (see also paragraph [0044]). As discussed above, one exemplary approach that may be used to determine an appropriate amount of antimicrobial agent to use is provided in Example 4.

In view of the foregoing amendment and remarks, it is respectfully submitted that the claims are now in condition for allowance and eventual issuance. Such action is respectfully requested. Should the Examiner have any further questions or comments which need be addressed in order to obtain allowance, please contact the undersigned attorney at the number listed below.

Acknowledgement of receipt is respectfully requested.

Respectfully submitted,

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